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10/590,095

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Felipe A. Donate

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EXAMINER

GOUGH, TIFFANY MAUREEN

ART UNIT

PAPER NUMBER

1657

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PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

| | | | |
|------------------------------|--------------------------------------|--------------------------------------|--|
| Office Action Summary | Application No. 10/590,095 | Applicant(s) DONATE ET AL. | |
| | Examiner TIFFANY M. GOUGH | Art Unit 1657 | |

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 16 December 2009.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-11 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-11 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date <u>8/16/06, 10/2/06, 12/16/09</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Election/Restrictions

Applicant's election with traverse of species methyl and alkyl in the reply filed on 12/16/2009 is acknowledged. Upon further consideration, the election of species is hereby withdrawn. Claims 1-11 are pending and have been considered on the merits herein.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation

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under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-11 are rejected under 35 U.S.C. 103(a) as being unpatentable over the combination of each of Baniel (US 3556739) in view of each of Raghavarao et al., (Clean Techn Environ Policy, 2003), Persson et al., (J. Chem Tech Biotechnol, 1999), Ullmann et al. (AIChE Journal vol 41. 1995), Koch (US 4233210) as evidenced by Stephenson (J. Chem. Eng. Data, 1993) and Davison et al., (J. Chem and Eng. Data, 1966).

Applicant claims a method for extracting water from an aqueous solution of a protein comprising the steps of:(a) intermixing the aqueous solution of the protein, an enzyme or a therapeutic protein, with a sufficient quantity of at least one glycol ether at a temperature at least 30 centigrade degrees above the lower critical solution temperature (LCST) to form a suspension comprising a concentrated aqueous protein phase and a liquid organic phase comprising said at least one glycol ether and at least 10 percent water extracted from the aqueous solution of the protein, wherein the glycol ether has an inverse solubility in water, with the proviso that the solubility of the glycol ether in water is significantly less than the solubility of water in the glycol ether, and the glycol ether does not significantly deactivate the protein, and (b) separating the

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concentrated aqueous protein phase formed in step (a) from at least a portion of the liquid organic phase. Applicant claims the intermixing of the glycol ether with the aqueous solution of the protein in step (a) to be conducted at a temperature of from about -5°C to about 70°C. Applicant further claims in step (b), that a portion of the liquid organic phase is allowed to remain with the concentrated aqueous protein phase in an amount from about 1 to about 30 percent by weight or substantially all of the liquid organic phase is separated from the concentrated aqueous protein phase. The method further comprising the steps of: (c) heating the liquid organic phase obtained in step (b) to a temperature which is higher than the temperature in step (a) to form a suspension comprising an aqueous phase and a glycol ether phase, and (d) separating the glycol ether phase formed in step (c) from the aqueous phase., wherein in step (c) the liquid organic phase is heated at a temperature of from about 40°C to about 100°C. Applicant claims the concentrated aqueous protein phase obtained in step (b) is further contacted with a hydrophobic organic solvent and the aqueous phase obtained in step (d) is further contacted with a hydrophobic organic solvent. Applicant claims the glycol ether to be selected from the group consisting of tripropylene glycol ethyl ether, propylene glycol isopropyl ether, dipropylene glycol isopropyl ether, tripropylene glycol isopropyl ether, propylene glycol n-propyl ether, dipropylene glycol n-propyl ether, propylene glycol t-butyl ether, dipropylene glycol t-butyl ether, tripropylene glycol t-butyl ether, propylene glycol n-butyl ether, dipropylene glycol n-butyl ether, tripropylene glycol n-butyl ether, propylene glycol n-pentyl ether, propylene glycol n-hexyl ether, butylene glycol methyl ether, dibutylene glycol methyl ether, butylene glycol ethyl ether and

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dibutylene glycol ethyl ether, ethylene glycol n-butyl ether, ethylene glycol n-pentyl ether, ethylene glycol n-hexyl ether, ethylene glycol n-heptyl ether, ethylene glycol 2-ethylhexyl ether, diethylene glycol n-pentyl ether, diethylene glycol n-hexyl ether, diethylene glycol n-heptyl ether, triethylene glycol n-hexyl ether, ethylene glycol n-butyl ether acetate, propylene glycol isobutyl ether, dipropylene glycol isobutyl ether, tripropylene glycol isobutyl ether, ethylene glycol t-butyl ether, ethylene glycol isobutyl ether, ethylene glycol isobutyl ether acetate, and diethylene glycol n-butyl ether acetate, and blends thereof.

Baniel (US 3556739) teaches an extraction method comprising intermixing an aqueous solution of phosphoric acid with an organic solvent, glycol ether (abstract), at a temperature within the range of -5°C to about 70°C to bring about phase separations, separating the phases, and then heating the liquid organic phase at temperatures higher than the first temperature (col. 2, lines 10-72, col. 3, lines 1-28, 45-col. 4, whole column, col. 5, lines 1-23, example 3, col. 7, lines 1-11). Baniel teaches that the method can be used to extract a product from an aqueous solution with organic solvents like glycol ethers.

Baniel differs from the claimed invention in that they do not teach extracting water from aqueous solutions of proteins.

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Raghavarao teach aqueous two phase extraction methods using glycol ethers dependent on cloud point based on temperature (p. 136, introduction). They also teach the purification of enzymes and therapeutic proteins (p. 137, second col., p.138, 1st col.).

Persson teach the purification of recombinant pharmaceutical proteins using a thermoseparating aqueous two-phase system to recover the target protein from the water phase (abstract). Although Persson teach temperature-phase induced separation using a polymer system, they teach that the two phases are formed by heating an aqueous phase above a critical temperature, i.e. cloud point or LCST, to separate the target protein from the EOPO polymers (p. 239, 1st col. , section 2.2, , Fig. 1, p. 240, section 3.1. 3.2). They teach that thermoseparating polymers separate from water solution above a certain temperature, i.e. cloud point or LCST (section 3.1) and that such polymer can be used for bioseparation of proteins (3.2). They teach that such a method is cost-effective and an environmentally favorable downstream process (abstract).

Ullmann teach phase transition extraction methods using solvents with a critical point of miscibility. They teach that with the manipulation of temperature one can create regions where the solvents form two distinct phases. They teach that such method is fast, efficient and improves upon previous extraction methods where the products are often damaged (introduction, p. 4898, whole page).

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Koch (US 4233210) teach an protein extraction method comprising precipitating a protein fraction with glycol ether (abstract, col. 2, lines 28-41, col. 3, lines 1-60).

Stephenson and Davison teach the mutual solubilities of water and glycol ethers as well as the lower critical solution temperature.

At the time of the claimed invention, it would have been obvious to one of ordinary skill in the art to use an organic solvent such as glycol ether for aqueous protein extractions because thermoseparating phase separation methods are known in the art to be more cost-effective, fast and preserve the product during the extraction methods as suggested by Raghavarao, Persson, Koch and Ullmann. Further, glycol ethers are known in the art to be used in extraction phase methods as suggested by Baniel and Koch. Given the teachings and inherent properties disclosed by Stephenson and Davison, one of ordinary skill in the art would be capable of determining the temperature to perform such extraction processes as disclosed by Baniel, Raghavarao, Persson and Koch with a reasonable expectation of success in separating a concentrated aqueous protein phase from a liquid organic phase.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the “right to exclude” granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-11 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1, 4-8, 10-14, 16-20 of copending Application No. 10/590,185. Although the conflicting claims are not identical, they are not patentably distinct from each other because both applications are drawn to methods of extracting proteins from aqueous solution comprising intermixing a solution of protein with glycol ether at temperatures within the same claimed ranges to produce phase separations wherein the protein is recovered. It is noted that the claims of ‘185 require a fermentation broth, however, a fermentation broth is an aqueous solution, therefore anticipated by the instant application.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claims 1, 2, 5, 6, 8, 9, 11 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1,4,6,7,12 of copending Application No. 10/590,685. Although the conflicting claims are not identical, they are not patentably distinct from each other because both applications are drawn to methods of extracting compounds from aqueous solution comprising intermixing a solution of protein with glycol ether at temperatures within the same claimed ranges to produce phase separations wherein the protein is recovered. It is noted that the claims of '685 are drawn to separating a hydrophilic organic compound; however, proteins are known to be both hydrophilic and hydrophobic compounds.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Conclusion

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

Shinnar et al. (US 5628906)

Baniel et al. (US 4275234).

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Allen et al (Biotechnol. Prog., 2007, vol .23, p. 1163-1170).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to TIFFANY M. GOUGH whose telephone number is (571)272-0697. The examiner can normally be reached on M-F 8-5 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Weber Jon can be reached on 571-272-0925. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Ralph Gitomer/
Primary Examiner, Art Unit 1657

/Tiffany M Gough/
Examiner, Art Unit 1657